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EXAMINER	
FORD, ALLISON M	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/694,190	WOLFINBARGER ET AL.	
	Examiner	Art Unit	
	ALLISON M. FORD	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-16,19-27,29-46 and 68-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-7,9-16,19-27,29-46 and 68-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response of 5/12/2009 has been received and entered into the application file. Claims 1, 2, 4, 19-21, 24, 25, 29-31 and 34 have been amended; claims 8, 17, 18, 28 and 47-67 have been cancelled; claims 68-71 have been added as new.

Claims 1-7, 9-16,19-27, 29-46 and 68-71 remain pending in the current application, all of which have been considered on the merits. The previous requirement for election of species of the generic inventions has been withdrawn, all species have been examined.

Priority

Acknowledgement is made of applicants claim for priority under 35 USC 120 as a continuation-in-part to prior filed application 09/660,422 (filed 12 September 2000), now US Patent 6,743,574. However, it is noted that Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120, as discussed in the previous office action.

The effective filing date, for purposes of determining patentability, of the instantly claimed subject matter is considered to the filing date of the instant application: 28 October 2003.

Response to Arguments/Amendments

Applicants' arguments submitted 5/12/2009 have been fully considered, in combination with the amendments. Arguments pertaining to maintained rejections will be addressed below, as appropriate. Rejections/objections not repeated herein have been withdrawn.

Oath/Declaration

Applicants' comments regarding the declaration have been noted, and upon reconsideration it is agreed that the supplemental declaration, submitted 1/4/2008, is appropriate, and thus is accepted. Because the 1/4/2008 declaration is a new declaration for the instant application, and because the instant application is a continuation-in-part of the parent application, only one named inventor must be shared with the parent application. While it is understood that Ms. Alyce Linthurst-Jones is the inventors married name, it is still considered a distinct name from Ms. Alyce Linthurst; however, as a continuation-in-part, a 'new' inventor may be added. The objection to the oath/declaration is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Applicants have traversed the rejections under 35 USC 112, second paragraph on the grounds that the amendments to the claims obviate the rejections. This is found persuasive in part. The rejection of claims 4 and 29-31 are withdrawn, but claims 1 and 2 remain indefinite.

Claims 1-7, 9-16, 19-27, 29-46 and 68-71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 2 remain rejected because it is still unclear if the water is passed through a bed of hydrophobic adsorbent resin and anion exchange resin *prior* to use for washing the tissue, or *after*. As amended the current claim language reads: "…washing at least some cell lysis remnants from said extracted tissue with water passing through a bed of hydrophobic adsorbent resin and anion exchange resin to remove the cell lysis remnants," This language is confusing- is the water *passing* through the bed of resins, if so, how does water which *is passing* through a resin function to wash a solid tissue? If Applicants intend for the water being used to wash the extracted tissue to be water *which has been passed*

through a bed of hydrophobic adsorbent resin and anion exchange resin, such should be made clear. Appropriate correction is required.

All claims inherent this deficiency, and thus are rejected on the same grounds.

Claim 22 is considered indefinite because claim 22 requires the storage solution to comprise ultrapure, endotoxin-free[[,]] water or a water replacement agent; however parent claims 1 and 2 requires that the storage solution comprises a water replacement agent. It is thus unclear if claim 22 is attempting to broaden the scope of claims 1 and 2 such that the storage solution can comprise ultrapure, endotoxin-free water *as an alternative* to a water replacement agent. Clarification is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Applicants have traversed the rejections under 35 USC 103(a) based on primary reference Atala on the grounds that Atala does not disclose use of a storage solution comprising a water replacement agent commensurate in scope with the claims. Applicant asserts that a 'water replacement agent' is defined as a an agent that "replaces water in the base matrix structure of soft tissue and provides the hydrating functions of water in the tissue", and that none of distilled water, physiological buffer and culture medium read on such. Applicants assert none of the secondary references cure this deficiency.

Applicants' arguments have been fully considered, but are not found persuasive. The independent claims only require the storage solution to generically comprise "a water replacement agent", though claim 21 further defines the water replacement agent, a limiting definition must be present in the

specification to define terms in the claims. A review of the specification did not reveal an appropriately limiting definition of 'water replacement agent' to limit it to those species recited in claim 21, as currently amended. Therefore, in giving the term 'water replacement agent' its broadest reasonable interpretation, at least physiological buffer and culture medium, as disclosed by Atala, read on water replacement agents, as required by claims 1-4, 12-16, 19, 20, 22, 2-27, 29-46 and 68-71. The appropriateness of physiological buffer and culture medium as 'water replacement agents' is based on the fact that Atala discloses distilled water, physiological saline and culture medium as functional equivalents of distilled water which may be used as the equilibrating fluid.

With regards to claim 21, the amendment to claim 21 narrows the scope of water replacement agents, and thus the rejection of record has been modified to address the narrowed scope. However, the equilibrizing solutions of Atala still satisfy the limitations of claim 21, in that at least some of the culture media disclosed by Atala comprise water replacement agents in accordance with claim 21. Amongst the culture mediums which may be used as the equilibrizing solution (storage solution) disclosed by Atala is RPMI 1640 medium (See Atala, col. 7, ln 51-58, referencing list of buffers and culture media disclosed at col. 6, ln 3-22); RPMI 1640 medium comprises glucose, proline, hydroxyproline, and i-inositol (a polyol), each of which are listed as water replacement agents in claim 21 (See RPMI 1640 Recipe). Therefore the rejections of record, modified to incorporate the RPMI 1640 recipe, are still deemed appropriate.

Claims 1-4, 12-16, 19-27, 29-46 and 68-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Atala (US Patent 6,376,244), in light of the RPMI 1640 recipe (Joslin.org Website), and in view of Wolfinbarger, Jr (US Patent 6,024,735).

Atala disclose a process for decellularizing soft tissue organs for subsequent implantation into a mammalian system.

The method of Atala comprises mechanically agitating an isolated organ to disrupt cell membranes;

treating the mechanically agitated, isolated organ in a solubilizing fluid to extract cellular material from the organ (which Applicants call "extracting a soft tissue sample with an extracting solution") to produce an extracted organ;

washing the extracted organ in a washing fluid to remove cellular debris, to produce a substantially decellularized organ; and optionally

equilibrating the substantially decellularized organ in equilibrating fluid (which reads on a storing step) (See Atala, col. 2, ln 43-67).

Atala states the solubilizing fluid (which is considered to read on the extracting solution of the current claims) may be an alkaline solution having a detergent. A variety of detergents are disclosed, including sodium cholate and deoxycholates (See Atala, col. 3, ln 14-30). Sodium cholate and deoxycholate are cholic acid and deoxycholic acid in alkaline solution, and thus read on non-denaturing anionic detergents as defined by the instant invention. In Example 1 Atala carry out the solubilization (extraction) step at a temperature of 4°C (See Atala, col. 9, ln 55-65). (relevant to claims 1, 2, 12, 26, 27, 43, 44, 68)

Atala states the washing fluid may be distilled water, physiological buffer or culture medium (See Atala, col. 3, ln 31-34). The distilled water used by Atala is considered to be chemically identical to water which has been passed through a bed of hydrophobic adsorbent resin and anion exchange resin (as required by the current claims), as both waters are free of impurities. (relevant to claims 1 and 2) The step of processing the water prior to use is considered to be a product-by-process limitation. Product-by-process limitations are considered only insofar as the method of production imparts distinct structural or chemical characteristics or properties to the product. Therefore if the product, as claimed, is the same or

obvious over a product of the prior art (*i.e.* is not structurally or chemically distinct), the claim is considered unpatentable over the prior art, even though the prior art product is made by a different process. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985), and *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979).

Atala state the equilibrating solution (considered to read on the storage solution of the current claims) may comprise distilled water, physiological buffer and culture media (See Atala, col. 2, ln 64-67). Physiological buffer and culture media are considered to read on water replacement agents, as they are disclosed along with distilled water as suitable solutions which may be used. Since physiological buffer and/or culture medium can be used as alternatives to distilled water, they are thus appropriately considered 'water replacement agents.' (relevant to claims 1, 2 and 22) It is further submitted that amongst the culture mediums which may be used as the equilibrating solution (storage solution) disclosed by Atala is RPMI 1640 medium (See Atala, col. 7, ln 51-58, referencing list of buffers and culture media disclosed at col. 6, ln 3-22); RPMI 1640 medium comprises glucose, proline, hydroxyproline, and i-inositol (a polyol), each of which are listed as water replacement agents in claim 21 (See RPMI 1640 Recipe). (relevant to claims 1, 2 and 21)

It is noted that the method of Atala is reported to *substantially* decellularize the organ (See Atala, col. 2, ln 59-63 & claim 1); as such it is a reasonable interpretation that at least some cell lysis remnants remain in the final product. These cell lysis remnants are considered to read on "cellular elements capable of inducing graft repopulation with an appropriate cell type" as required by the instant inventions.

The method of Atala differs from the method of the current claims in that they do not teach using pressure meditated flow of the solubilizing fluid (extracting solution), washing fluid or the storage solution when preparing the organ. However, it is submitted that use of pressure mediated flow of the

solutions was recognized as conventional in the art, at the time the invention was made (See Wolfinbarger, Jr), and thus application of such in the method of Atala would have been *prima facie* obvious. For example, Wolfinbarger, Jr disclose several recirculation methods whereby solutions are flushed through a graft material using positive and negative pressure (See Wolfinbarger, Jr, col. 13, ln 6-col. 19, ln 36). One of ordinary skill would have had a reasonable expectation of successfully applying the pressure mediated recirculation methods of Wolfinbarger, Jr to the process of Atala because the pressure mediated recirculation methods of Wolfinbarger, Jr involve simple mechanics of applying positive and negative pressures to fluids to flush a material. The pressure mediated flow and recirculation methods could have routinely been applied to either, or all of, the solubilizing fluid (extracting solution), washing solution or the storage solution of Atala. (claims 1-4, 13-15)

The method of Atala further differs from the method of the current claims in that they do not teach including a decontaminating agents in the solubilizing (extracting) solution or in the storage solution. However, Wolfinbarger, Jr teach including decontaminating agents in detergent solutions intended to remove cellular lysis remnants from tissues and in storage solutions for storing decellularized tissues intended for subsequent use in implantation procedures to improve sterility (See Wolfinbarger, Jr, col. 11, ln 37-47 & col. 22, ln 53-55). The decontaminating agent may be one or more of antibiotics, antiviral agents, hydrogen peroxide, alcohols, such as methyl, ethyl, propyl, isopropyl, butyl, t-butyl, and sodium hydroxide (See Wolfinbarger, Jr. col. 6, ln 54-65). It is submitted that appropriate decontaminating agents and appropriate concentrations thereof would have been routinely optimized by one of ordinary skill in the art based on the tissue source and the level of suspected contamination (claims 19, 20, 23-25, 34, 69, 71) The obviousness of optimization of the concentrations is based on the legal precedent established in *In re Aller* which held that differences in concentration will not support

patentability unless there is evidence that the claimed concentration is critical. See *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

It is further noted, to improve sterility and reduce contamination, Wolfinbarger, Jr suggest use of endotoxin-free, deionized/distilled water (See Wolfinbarger, Jr col. 6, ln 1-2). One of ordinary skill in the art would have recognized the desirability of using USP grade, ultrapure, endotoxin free water for applications wherein the product is intended for implantation into mammalian systems, and thus use of such water would have been *prima facie* obvious in the method of Atala. (claim 16).

Some of the parameters and conditions required by the instant claims are not specifically disclosed by Atala or Wolfinbarger, Jr, specifically the concentration/amount of the detergent used in the solubilizing (extracting) fluid of Atala, the duration of the solubilizing (extracting) step, the temperature at which the solubilizing (extraction) is to be carried out, or the flow rate of the pressure mediated flow; however each of these parameters are recognized as result effective variables that directly affect the degree to which the organ is decellularized, and the extent to which the native structure of the matrix is retained. As result effective variables, each of these parameters would have been routinely optimized by one of ordinary skill in the art at the time the invention was made. "[W]here the general conditions of a claim are disclosed by the prior art it is not inventive to discover the optimum or workable ranges by routine experimentation" See *In re Aller* (supra).

With regards to the conditions under which the solubilizing (extracting) step is carried out, Atala states the concentration of detergent in the solubilizing fluid is a result effective variable, and would be varied based on the tissue being treated (See Atala, col. 6, ln 48-58 & col. 7, ln 18-31). The concentration of a particular detergent would be routinely optimized by one of ordinary skill in the art in order to achieve the desired result of effectively removing cellular components, without disrupting the interstitial

structure of the organ, optimization would be based on the detergent and the tissue to be treated. It logically follows that the duration of the solubilization step (extracting step) would be recognized as a result effective variable that, too, would have been routinely optimized by one of ordinary skill in the art at the time the invention was made in order to achieve the desired result. (claims 29-33, 39-42). Optimization of the temperature is held to be *prima facie* obvious, this holding is based on legal precedent established in *In re Aller* (cited supra), that differences in temperature will not support patentability unless there is evidence that the claimed temperature is critical. (claims 45, 46)

With regards to the flow rate of the pressure mediated flow, Wolfinbarger, Jr further state the flow rate of the pressure mediated flow is a result effective variables (See Wolfinbarger, Jr col. 13, ln 53-col. 14, ln 6). The flow rate directly affects the extent of removal of cellular debris, as well as the extent of damage caused to the matrix structure. (claims 35-38)

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1-7, 9-16, 19-27, 29-46 and 68-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Atala (US Patent 6,376,244), in light of the RPMI 1640 recipe (Joslin.org website), in view of Wolfinbarger, Jr (US Patent 6,024,735), and further in view of Wolfinbarger, Jr (US Patent 6,432,712).

The teachings of Atala and Wolfinbarger, Jr ('735) have been set forth in detail above. Neither Atala nor Wolfinbarger, Jr ('735) disclose including an endonuclease in the solubilizing (extracting) solution. However, Wolfinbarger, Jr ('712) discloses using a broad spectrum, recombinant endonuclease BENZONASE™ to decellularize organs and tissues (See Wolfinbarger, Jr ('712), col. 8, ln 40-67). Because the method of Atala is intended to result in a decellularized organ, it would have been

prima facie obvious to one of ordinary skill in the art to include BENZONASE™ in the solution intended to remove cellular components from the organ. One would have had a reasonable expectation of successfully including BENZONASE, and determining an appropriate concentration, based on the teachings of Wolfinbarger, Jr ('712). (claims 5-7 and 9-11).

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting: Duplicate Claim Warning

Applicant is advised that should claim 32 be found allowable, claim 39 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 32 recites the same limitation as claim 39.

Double Patenting: Non-Statutory Obviousness-type

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 12-14, 16, 19-27, 29-33 and 68-71 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10, 12-14, 19, 20, 23-34 and 41 of U.S. Patent No. 6,734,018 (hereafter "the '018 Patent").

The '018 patent claims a process for preparing an acellular soft tissue graft for implantation into a mammalian system, consisting of:

(a)inducing a pressure mediated flow of an extracting solution comprising one or more nonionic detergents and one or more endonucleases, through soft tissue, to produce extracted tissue;

(b) inducing a pressure mediated flow of a treating solution comprising one or more anionic detergents through said extracted tissue, to produce a treated tissue;

(c) inducing a pressure mediated flow of a decontaminating solution comprising one or more decontaminating agents through said treated tissue, to produce said acellular soft tissue graft; and

(d) storing said acellular soft tissue graft in a storage solution comprising one or more decontaminating agents.

Noting the instant claims use the open transitional language 'comprising', the claimed method permits additional steps (such as the initial extracting step (a) of the '018 patent), as such, the method of the '018 patent is considered to render obvious the instantly claimed method.

In the '018 patent step (b) of inducing a pressure mediated flow of a treating solution comprising one or more anionic detergents through the tissue is considered to read on the claimed method step of extracting the soft tissue with a non-denaturing anionic detergent to produce an extracted tissue. Claims 23-29 of the '018 patent define the anionic detergent as being identical to that used in the instant method, both in composition and concentration; thus the effect on the soft tissue is inherently the same. (relevant to instant claims 1, 2, 3, 12, 26, 27, 29-

31, 68) Claim 12 of the '018 patent states the treating solution may be recirculated through the graft (relevant to instant claim 13).

In the '018 patent step (c) of inducing a pressure mediated flow of a decontaminating solution comprising one or more decontaminating agents through said treated tissue is considered to read on the claimed method steps of washing at least some cell lysis remnants from the extracted tissue with water. Claim 41 of the '018 patent explicitly requires a washing step with said decontaminating solution. Please note that claim 29 defines the decontaminating solution as comprising ultrapure, endotoxin-free water; again ultrapure, endotoxin-free water is considered identical to water which has been passed through a hydrophobic adsorbent resin and anion exchange resin (there is no requirement in the instant claims that excludes additional agents, such as decontaminating agents, from being further provided to the washing solution). (relevant to instant claims 1, 2 and 16).

In the '018 patent step (c) of inducing a pressure mediated flow of a decontaminating solution comprising one or more decontaminating agents through said treated (and optionally washed) tissue is considered to further read on the claimed method step of inducing a pressure mediated flow of storage solution comprising a water replacement agent. Claim 32 of the '018 patent defines the decontaminating agents as including glycerol; glycerol is amongst those agents listed as a water replacement agent. (relevant to instant claims 1, 2, 21, 22) Claim 13 of the '018 patent recites the decontaminating solution (which reads on the storage solution of the instant claims) may be recirculated through the graft. (relevant to instant claim 14)

Finally, in the '018 patent step (d) of storing said acellular graft in a storage solution comprising at least one decontaminating agent reads on the claimed method step of storing the acellular tissue in a storage solution. Again the storage solution in the '018 patent can include ultrapure endotoxin free water

(See '018 claim 30) and further comprise decontaminating agents such as antimicrobial agents chlorine dioxide, ethanol, methanol, isopropanol and glycerol (See '018 claim 31-33) (relevant to instant claims 19, 20, 69-71). It is further submitted that appropriate decontaminating agents and appropriate concentrations thereof would have been routinely optimized by one of ordinary skill in the art based on the tissue source and the level of suspected contamination. The obviousness of optimization of the concentrations is based on the legal precedent established in *In re Aller* which held that differences in concentration will not support patentability unless there is evidence that the claimed concentration is critical. See *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). (relevant to instant claims 23, 25) Glycerol is also a water replacement agent, as defined by the instant claims (relevant to claims 1, 2, 21, 22).

Therefore the prior patent renders the instant claims *prima facie* obvious.

Claims 1-3, 12, 19, 20, 22-27, 29-31 and 68-71 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6-10, 13-15, 22 and 23 of U.S. Patent No. 7,338,757 (hereafter "the '757 Patent") in view of Wolfinbarger, Jr (US Patent 6,024,735; hereafter "Wolfinbarger, Jr").

The '757 patent claims a process for preparing an acellular soft tissue graft comprising:

(a) extracting at least one soft tissue sample with a buffered alkaline extraction solution which contains at least one nonionic detergent and at least one endonuclease, and which is hypotonic to the cells in said soft tissue sample,

(b) washing said extracted tissue in a first washing solution comprising water to produce a first washed tissue,

(c) treating said first washed tissue with a first processing solution comprising an anionic detergent to produce a first processed tissue,

(d) washing said first processed tissue in a second washing solution comprising water to produce a second washed tissue, and

(e) storing said second washed tissue in a storage solution comprising at least one decontaminating agent and water.

Noting the instant claims use the open transitional language 'comprising', the claimed method permits additional steps (such as the initial extracting step (a) of the '757 patent), as such, the method of the '757 patent is considered to render obvious the instantly claimed method. The '757 patent does not utilize a denaturing detergent (noting both nonionic and anionic detergents are non-denaturing) (relevant to instant claim 3)

In the '757 patent step (c) of treating the washed tissue with the first processing solution comprising an anionic detergent is considered to read on the claimed method step of extracting the soft tissue with a non-denaturing anionic detergent to produce an extracted tissue. Claims 6-9 of the '757 patent define the anionic detergent as being identical to that used in the instant method, both in composition and concentration; thus the effect on the soft tissue is inherently the same. (relevant to instant claims 12, 26, 27, 29-31, 68) Claim 22 of the '757 patent states the treating step involves subjecting the tissue to a pressure mediated flow of the first processing solution (relevant to instant claim 2).

In the '757 patent step (d) of washing the first processed tissue in a washing solution comprising water is considered to read on the claimed method step of washing at least some remaining cell lysis remnants from the extracted tissue with water. It is noted that the '757 patent does not define the water as being water which has been pass through a hydrophobic adsorbent resin and anion exchange resin; however, it is submitted that use of USP grade, endotoxin-free,

deionized/distilled water, which is considered to be equivalent to water which has been passed through hydrophobic adsorbent resins and anion exchange resins, would have been *prima facie* obvious to one of ordinary skill in the art. USP grade, endotoxin-free, deionized/distilled water is routinely used in the art in processes relating to biological matter where sterility and contamination are a concern (see, e.g. Wolfinbarger, Jr col. 6, ln 1-2). Furthermore, claim 23 of the '757 patent states the washing step involves subjecting the processed tissue to a pressure-mediated flow of said water (washing) solution (relevant to instant claim 2).

Finally, in the '757 patent step (e) of storing the washed tissue in a storage solution comprising at least one decontaminating agent clearly renders obvious the claimed method step of storing the washed tissue in storage solution comprising decontaminating agents. Claims 14 and 15 of the '757 patent define the decontaminating agent as an antimicrobial agent, such as chlorine dioxide, ethanol, methanol, or glycerol. (relevant to instant claims 19, 20, 24, 69-71). Glycerol, at least, is also considered to read on a water replacement agent present in the storage solution. (relevant to instant claims 1, 2, 22) It is further submitted that appropriate decontaminating agents and appropriate concentrations thereof would have been routinely optimized by one of ordinary skill in the art based on the tissue source and the level of suspected contamination. The obviousness of optimization of the concentrations is based on the legal precedent established in *In re Aller* which held that differences in concentration will not support patentability unless there is evidence that the claimed concentration is critical. See *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). (relevant to instant claims 23, 25)

The claims of the '757 patent differs from the current claims in that the patented claims do not recite applying a pressure meditated flow of the storage solution. However, because the '757 patent does teach use of pressure mediated flow of the extracting, processing and washing solutions (See claims 21-23) it is submitted that use of pressure mediated flow of the storage solutions would have been obvious as well. (relevant to instant claims 1, 2)

Therefore the prior patent renders the instant claims *prima facie* obvious.

Claims 1-4, 12-16, 19-21, 26, 27 and 68-71 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 and 10-16 of copending Application No. 12/475,217 (hereafter "application '217").

This is a provisional obviousness-type double patenting rejection.

Claims 1-8 and 10-16 of copending application '217 are identical to the instant claims except the copending claims 1 and 2 generically refer to the extracting solution as comprising a non-denaturing detergent, not an anionic non-denaturing detergent. However, claim 15 of the copending application '217 defines the non-denaturing detergent as N-lauroyl sarcosinate, deoxychloic [*sic*: deoxycholic] acid, taurocholic acid, glycocholic acid, cholic acids, and combinations thereof. These species are all examples of anionic detergents, and are identical to the species recited in current claim 68.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALLISON M. FORD whose telephone number is (571)272-2936. The examiner can normally be reached on 8:00-6 M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Allison M. Ford/
Primary Examiner, Art Unit 1651